SCIENTIFIC LETTER

Plasma C reactive protein concentration indicates a direct relation between systemic inflammation and social deprivation

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Social deprivation is a major factor in health inequality. In the UK residence in a socially deprived area is associated with an increase in mortality from coronary heart disease (CHD).[1] A positive association between the incidence of CHD and residence in a socially deprived neighbourhood has also been observed in the USA.[2]

Inflammation is important in the development of atherosclerosis, plaque rupture, and thrombosis leading to myocardial infarction. An increase in the plasma concentration of C reactive protein (CRP), within the reference range for the population but below the threshold that indicates clinically significant inflammation, is an independent risk factor for CHD.[3] It is also a predictor for the development of diabetes mellitus[4]—a major cause of vascular disease. We have investigated the relation between the plasma CRP concentration and social deprivation in two large study populations.

METHODS AND RESULTS

CRP was measured by an enzyme linked immunoassay, with a lower limit of the working range of 0.1 mg/l, calibrated with the international reference standard (CRM 470-CAP/IFCC; lot 91/0619) and thus yielded results comparable with other major studies.[3] CRP measurements were available for 5245 men aged 45–64 years on recruitment in 1989–91 to the WOSCOPS (West of Scotland coronary prevention study).[4] The second population were men (n = 941) and women (n = 1160) aged 30–59 years studied in 1996 for the Midspan family study.[5]

The deprivation status of the subjects was assessed from the postcode of residence, obtained from the 1991 census data, according to Carstairs and Morris, which defines seven categories of deprivation, category 1 being the most affluent.[1] The deprivation score (DEPCAT) for an area of residence is calculated from the population census data on car ownership, overcrowded housing, occupations of the household heads, and percentage of men unemployed. In the UK a national census is undertaken every decade. The DEPCATs derived from the 1991 national census were used in this study as it was closest in time to the recruitment for both population studies. Full details of the methods used to derive the DEPCATs are available on line from the Medical Research Council's Social and Public Health Sciences Unit at the University of Glasgow (www.msoc-mrc.gla.ac.uk/Publications/pub/Carstairs_MAIN.html), which has reported that the DEPCATs of Scottish postcode sectors based on the 2001 census data are strongly correlated ($r = 0.955$) with those derived from the 1991 census.

The plasma concentration of CRP was log normally distributed in the population. Table 1 gives the geometric mean CRP concentration for the WOSCOPS population grouped by deprivation and smoking status. The mean CRP concentration in current smokers was about twice that of the corresponding never smokers and in the most deprived was about double that observed in the most affluent. The trend was present among the former smokers though they were heterogeneous with regard to the time since they stopped smoking. The Midspan population data show an increase in CRP among both men and women with increasing deprivation. In both populations univariate analysis showed a highly significant correlation between plasma CRP and deprivation ($p < 0.0001$).

Table 2 gives the CRP concentration in the WOSCOPS population grouped by deprivation, smoking, and body mass index (BMI). The data show a highly significant increase in CRP ($p < 0.0001$) with increasing deprivation.

Inflammatory disorders, cigarette smoking, obesity (assessed by BMI), age, sex, and use of drugs such as aspirin, angiotensin converting enzyme inhibitors, and statins influence CRP. Table 3 gives the results of regression modelling, which showed that taking all these factors into account for

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CRP, C reactive protein; DEPCAT, deprivation score; WOSCOPS, West of Scotland coronary prevention study

Table 1 Geometric mean C reactive protein (mg/l) in WOSCOPS (West of Scotland coronary prevention study) and Midspan family study participants grouped according to deprivation score (DEPCAT)

		DEPCAT						
Study	**Subgroup**	**1**	**2**	**3**	**4**	**5**	**6**	**7**
WOSCOPS	NS	0.83 (52)	1.06 (167)	1.12 (300)	1.19 (258)	1.15 (241)	1.23 (141)	1.57 (88)
	FS	1.30 (91)	1.42 (206)	1.32 (507)	1.62 (378)	1.62 (361)	1.65 (300)	1.65 (141)
	CS	1.42 (78)	2.41 (217)	2.16 (531)	2.34 (517)	2.29 (503)	2.83 (424)	3.03 (292)
Midspan family study	Men	0.72 (78)	0.74 (136)	0.92 (227)	0.81 (189)	0.99 (107)	0.98 (192)	0.88 (12)
	Women	0.68 (95)	0.77 (156)	0.93 (282)	0.89 (239)	1.04 (167)	1.20 (212)	1.68 (9)

Numbers of subjects in each group are given in parentheses.
DEPCAT 1 most affluent, DEPCAT 7 most deprived.
The WOSCOPS subjects, all men, are grouped according to history of smoking: NS, never smoker; FS, former smoker; CS, current smoker.

Table 2 Geometric mean C reactive protein (mg/l) in WOSCOPS participants grouped according to smoking status, DEPCAT, and quartile of body mass index (BMI)

	Never smokers by BMI quartile				Current smokers by BMI quartile			
DEPCAT	I	II	III	IV	I	II	III	IV
1	0.68	0.63	1.05	1.15	1.25	1.06	1.39	2.41
2	0.77	0.97	1.20	1.49	2.48	2.03	2.27	3.32
3	0.85	0.90	1.22	1.63	1.80	2.14	2.36	2.83
4	0.84	1.19	1.19	1.55	2.08	2.18	2.51	2.69
5	0.63	1.09	1.54	1.62	2.14	1.86	2.32	3.13
6	0.94	0.94	1.12	1.99	2.46	2.72	3.00	3.32
7	1.07	1.48	1.63	1.95	2.64	3.25	3.39	3.22

BMI quartile I, $\leqslant 23.83\ kg/m^2$; II, >23.83 and $\leqslant 25.65\ kg/m^2$; III, >25.65 and $\leqslant 27.76\ kg/m^2$; IV, $>27.76\ kg/m^2$.

Table 3 Model estimated percentage increase in C reactive protein (95% confidence interval) associated with a one unit difference in DEPCAT

		Adjustments				
Study	Subgroup	Age only	Age and smoking	Age and BMI	Age and medication	Age, smoking, BMI, and medication
WOSCOPS		8.3 (6.5 to 10.2) p<0.0001	6.1 (4.3 to 7.9) p<0.0001	7.9 (6.1 to 9.8) p<0.0001	8.3 (6.4 to 10.1) p<0.0001	5.4 (3.6 to 7.1) p<0.0001
Midspan family study	Men	6.4 (1.4 to 11.5) p=0.011	4.5 (−0.3 to 9.50) p=0.067	4.9 (0.2 to 9.8) p=0.039	6.1 (1.2 to 11.2) p=0.014	2.3 (−2.2 to 7.0) p=0.31
	Women	11.3 (6.2 to 16.7) p<0.0001	11.2 (6.0 to 16.7) p<0.0001	6.1 (1.6 to 10.7) p=0.0067	10.6 (5.6 to 15.9) p<0.0001	4.8 (0.4 to 9.5) p=0.033

Age and BMI are included in models as linear continuous effects. Smoking is included in models as a three level categorical variable (never, former, current). Medications is included as a binary variable, indicating use of aspirin, angiotensin converting enzyme inhibitors, or statins (note that no WOSCOPS participants were taking statins at baseline).

the WOSCOPS population maintained a highly significant relation ($p < 0.0001$) between deprivation and CRP with an increase in CRP of 5.4% (95% confidence interval 3.6 to 7.1) for each unit of deprivation. In the Midspan population the relation was observed for both sexes combined, with each unit of deprivation associated with an increase in CRP of 3.7% (95% confidence interval 0.5 to 7.0%, $p = 0.024$). Positive associations were observed for women and men separately (table 3), and though the association did not reach significance for men, this may have been a consequence of reduced sample size, since there was no evidence that the effect of deprivation was different for men and women (interaction test for heterogeneity, $p = 0.62$).

DISCUSSION

Social and economic deprivation, assessed by place of residence, is associated with an aggregation of features that results in an increase in low grade background systemic inflammation indicated by an increase in the plasma concentration of CRP that is not fully explained by smoking and BMI. Background inflammation may partially explain the increase in morbidity and mortality from CHD observed in the socially and economically deprived sections of the population.

In this cross sectional study of two populations it is not possible to identify with any degree of confidence what factors associated with deprivation caused the observed increase in background inflammation. One could speculate that it may be due to low grade subclinical infections caused by factors such as over crowding in poor quality damp housing with suboptimal personal and dental hygiene.

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D O'R conceived of measuring C reactive protein (CRP) in both studies, wrote the first and final versions of the paper, and is the guarantor. D O'R, M N U, G C M W, and C J P conceived of the idea of analysing the relation between CRP and deprivation. G C M W conceived of the Midspan family study, M N U was the principal investigator, and A M performed the statistical analysis for Midspan. C J P was Study Director for WOSCOPS, M C coordinated CRP analysis, and M R and J N performed the statistical analysis for WOSCOPS.

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IMAGES IN CARDIOLOGY

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Widespread ST segment elevation caused by cerebral infarction

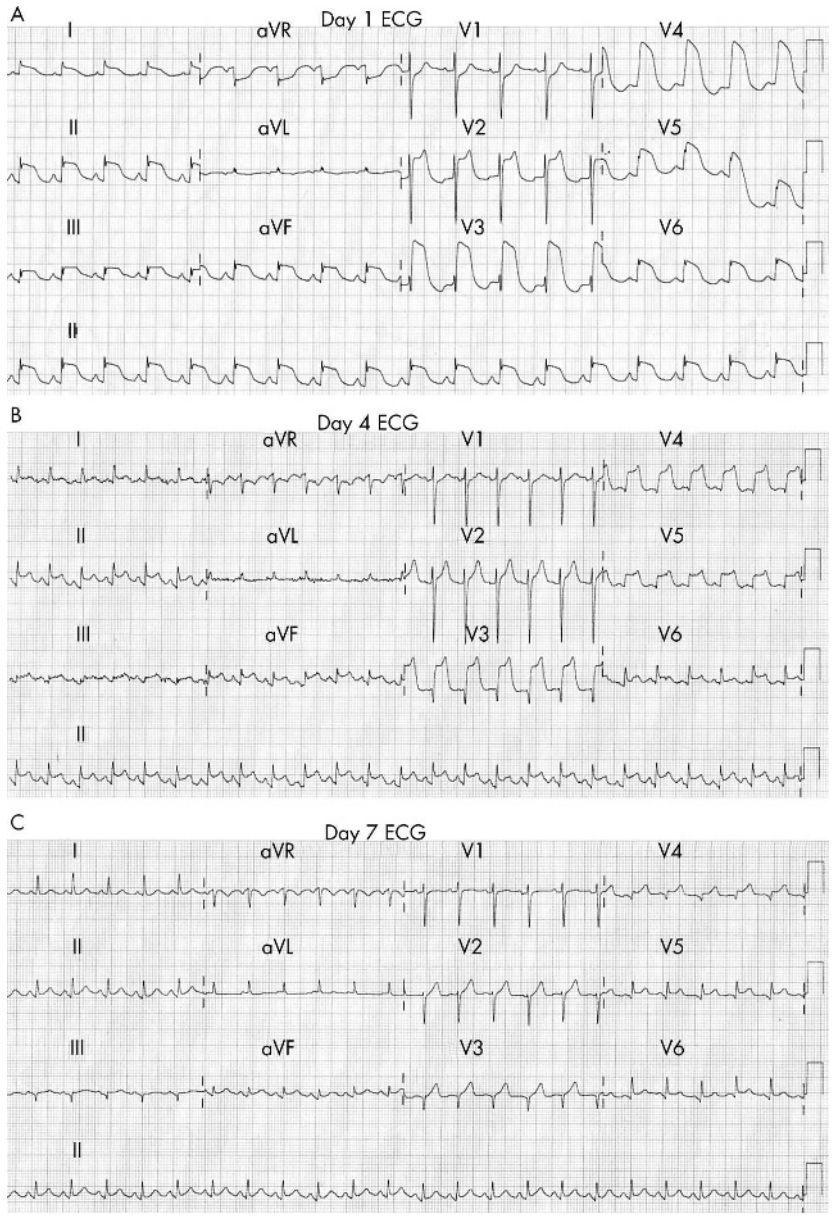
A 44 year old Chinese woman was found unconscious at home. She had known hypertension, peripheral vascular disease, schizophrenia, and craniotomy for traumatic intracranial haemorrhage. She had spontaneous breathing, rate 16 resps/min, blood pressure 134/100 mm Hg, pulse 112 beats/min, and oxygen saturation 95% (ambient air). Bowel and urinary incontinence were noted. There was no physical response to pain, and plantar responses were equivocal. The pupils were normal and reactive. No focal neurological signs were present. The rest of the examination was unremarkable.

The ECG showed sinus rhythm with widespread convex ST segment elevation in leads I, II, III, aVF and V2–6, suggestive of extensive myocardial infarction (panel A). Serum electrolytes were normal. A computed tomographic (CT) brain showed periventricular ischaemia, and an old right basal ganglia infarct without haemorrhage.

Coronary angiography revealed normal arteries without vasospasm and an echocardiogram showed normal ventricular systolic function. An electroencephalogram (EEG) on day 3 showed right temporal epileptogenic activity, with diffuse encephalopathy. Toxicology screen was negative.

The patient remained comatose, developed rhabdomyolysis, and acute renal failure. Magnetic resonance imaging (MRI) of the brain on day 6 showed infarction of the entire right cerebral hemisphere, left frontal lobe, and bilateral thalami. A repeat EEG on day 7 showed severe, diffuse encephalopathy. ST segment elevations on ECG nearly resolved on day 7 (panels B and C), a day before the patient died.

We believe the patient had status epilepticus resulting in multi-organ failure. The ECG changes were likely due to extensive brain infarction caused by status epilepticus. The postulated mechanism is excessive sympathetic tone and catecholamine production, leading to myocardial injury with ECG changes. We believe this is a rare case of severe cerebral infarction resulting in massive ST segment elevation, mimicking extensive myocardial infarction.



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